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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FOLEY, SHANON A	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/103,262	BERMAN ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-23 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-23 and 26-30* is/are rejected.

7)☒ Claim(s) *20 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 June 1998* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/1/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The examiner of your application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648, Examiner Foley.

Election/Restrictions

Applicant's election without traverse of group V, claims 19-23 and the election of 6E10 in the paper received October 20, 2003 is acknowledged. Applicant's arguments regarding the examination of 26-28, 29 and 30 is found persuasive. Therefore, claims 19-23 and 26-30 are pending and under consideration. Since the prior art does not teach the elected monoclonal antibody (Mab) 6E10, a prior art search was also carried out for Mabs 13H8, 6D8, 5B3, and 5B6.

Information Disclosure Statement

The information disclosure statement filed June 1, 2000 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The references listed that have a corresponding copy in one of the parent applications have been considered and initialed. If a reference copy was not located, the corresponding citation on the 1449 has been struck through. Applicant is required to provide a copy of the references that cannot be located with the next correspondence, if consideration is desired.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The abstract of the disclosure is objected to because it does not reflect the concepts claimed. Correction is required. See MPEP § 608.01(b).

The specification is objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific amino acid sequences comprising four or more amino acids and ten or more nucleic acids in the specification. Specific examples within the specification that do not comply with the sequence rules are found in the description of Figure 2, page 9, line 8 and page 57, lines 23-24. Applicant is required to append a SEQ ID NO. to any sequence applicable to the rule. See 37 CFR § 1.821 (a)-(d) and MPEP § 2422. Appropriate correction is required.

Drawings

Figure 4 is objected to because the immunoblot lanes are handwritten and illegible. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Priority

Examiner acknowledges Applicant's preliminary amendment to the first page of the specification updating continuing data. The status of related applications should be updated to ensure a complete file record. Furthermore, Applicant is required to request a corrected filing

receipt setting forth the continuation data and the relationship of the parent applications to the instant application to properly complete the file wrapper.

Claim Objections

Claims 20 and 21 are objected to because of the following informalities: "AND" in the last line of each claim should not be capitalized. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19 and 26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 19 and 26 as written, do not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP § 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19 and 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 requires that the instant antibody, or epitope-binding fragment thereof "has the characteristics" of a monoclonal antibody selected from 6E10, 13H8 and 6D8. Claim 26 also recites the same "characteristics" of the antibodies and the epitope-binding fragments as claim 19. Although the specification teaches general characteristics of the antibodies disclosed on page 5, lines 17-25, the data presented in Table 3 on page 58 and Table 4 on page 61, demonstrate that antibodies 6E10, 13H8 and 6D8 exhibit different affinities, bind to different epitopes and have different activities. Therefore, each of the antibodies possess different characteristics. Due to the difference in structural and functional features disclosed for each of the instant antibodies claimed, the "characteristics" of the instant antibody or epitope-binding fragment is indeterminable. This rejection also affects dependent claims 27-30.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 19 and 26-30 encompass antibodies or epitope-binding fragments thereof that have the "characteristics" of monoclonal antibodies 6E10, 13H8 and 6D8. However, the disclosure does not adequately describe the "characteristics" of these antibodies. Therefore, the skilled artisan would be unable to identify an antibody or an epitope-binding fragment thereof with the same "characteristics" as those instantly claimed.

On page 5, lines 17-25, the specification states that the monoclonal antibodies are characterized by affinity for a ligand, epitope binding and the ability to block CD4/gp120 binding, neutralize HIV virions, reduce reverse transcriptase in vitro and inhibit syncytia formation. Additionally, the disclosure states that the monoclonal antibodies are specific for the internal clip site within gp120. However, the disclosure does not teach any particular strength of affinity for any of the antibodies. Nor does the disclosure identify an epitope that the instant antibodies bind to. On page 56, lines 17-21, the specification states that the majority of the Mabs define 11 epitopes of gp160 and that the epitopes recognized by these Mabs are linear. The disclosure also suggests that 6E10 binds to a conformational epitope. However, the exact epitopes the instant antibodies bind to is not disclosed. The specification only teaches that randomly expressed portions of the gp160 and gp120 were used for epitope mapping, see page 57, lines 1-34. Table 3 on page 58 depicts antibodies in italics that were raised against gp120. Non-italicized Mabs were raised against gp160. The Table also appears to list the specific amino acid residue(s) that corresponds to the epitope each Mab binds to. However, there is no numbering provided for which residue listed corresponds to which amino acid within the randomly expressed portions of gp120 or gp160 the antibodies were raised against. Therefore, the skilled artisan would be unable to identify an antibody or an epitope-binding fragment that

binds to the same epitope as the instantly claimed Mabs because the epitopes of the instant Mabs have not been defined. In addition, each of the antibodies have different functional characteristics according to the data presented in Table 4 on page 61 and the discussion section following. Therefore, the disclosure lacks an adequate written description of the epitope and the "characteristics" required by the antibodies or epitope-binding fragments claimed.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there is no identification of the epitope that each Mab binds to, or structural or functional "characteristics" defining the instant antibodies. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the structure or "characteristics" of the genus of antibodies or epitope-binding fragments claimed due to the lack

of sufficient identification of the epitopes the instant Mabs bind to and the lack of "characteristics" that unify the antibodies claimed.

Therefore, only Mabs 6E10, 13H8 and 6D8, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 19-23 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The examiner acknowledges applicant's preliminary amendment to the specification updating the ATCC designations and dates of deposit. However, while the claims and the ATCC deposit receipt list "13H**8**" as deposited, the statement under 37 CFR §§ 1.804(b) and 1.808(a)(2) regarding the deposit list "13H**B**" (emphasis added). It is presumed that the statement contains a typo regarding this antibody. However, the statement is considered defective with respect to this antibody until a corrected statement is submitted.

Claims 19 and 29 indicate that 6D8 is produced by a hybridoma with ATCC accession number CRL 10513. However, the statement by applicant under 37 CFR §§ 1.804(b) and 1.808(a)(2) indicates that the accession number CRL 10513 corresponds to "10D8". It is unclear if this is also a typo because both 10D8 and 6D8 are disclosed in the specification. In any case, the proper deposit information regarding 6D8 is incomplete.

There is no indication that the hybridoma cell lines corresponding to antibodies 5B6 or 6D8 recited in the claims have been deposited. It is apparent that the hybridomas required to make these antibodies are required to practice the claimed invention because the hybridomas specifically make the designated antibodies required by the claims. Therefore, the hybridomas corresponding to each of the antibodies are a necessary limitation for the success of the invention as stated in the claims. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, a deposit may satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See 37 CFR § 1.802. One cannot practice the claimed invention without antibodies recited. One cannot determine whether an antibody has the necessary characteristics without access to the instant antibodies disclosed. Therefore, access to hybridomas that make each of the antibodies claimed is required to practice the invention. The specification does not provide a repeatable method for readily identifying antibodies without access to the hybridoma or corresponding antibody and these components do not appear to be readily available material.

Deposit of the hybridomas corresponding to each of the recited antibodies in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112, because the cells would be readily available to the public to practice the invention claimed, see 37 CFR § 1.801-37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating

that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR § 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR § 1.809(d) should be added to the specification. See 37 CFR § 1.803 - 37 CFR § 1.809 for additional explanation of these requirements.

Claims 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing an immune response with Mab 5B3, 5B6, 6E10, 13H8 or 6D8, the specification does not reasonably provide enablement for inducing a therapeutic or prophylactic immune response against HIV with these antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims or make antibodies 13H8, 6D8 or 5B6.

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of skill of one in the art;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claim 21 is drawn to a composition comprising a monoclonal antibody selected from 5B3, 5B6, 6E10, 13H8 or 6D8 in a sterile pharmaceutical vehicle that is suitable for administration to a patient. Claim 22 additionally requires that the antibody is conjugated to a toxin. Claim 23 is drawn to a method of administering a therapeutically acceptable dose of the Mabs listed in claim 21 to a patient having or at risk of having HIV infection.

The nature of the invention

The nature of the invention is a therapeutic or prophylactic composition and a method of treating or preventing HIV infection. The nature of the invention is derived from the recitation of claim 23 and discussions throughout the disclosure, such as lines 10-11 of page 4.

The state of the prior art

The instant Mabs are specific for gp160 or gp120, see Tables 3 and 4. The state of the prior art clearly indicates that a humoral and cellular immune response is observed in chimpanzees inoculated with a recombinant gp120 protein. The antibodies generated against the recombinant gp120 neutralized HIV infectivity *in vitro*. However, the immune response elicited against this protein was insufficient for preventing HIV infection upon challenge. See Berman et al. (PNAS. 1988; 85 (14): 5200-4, provided in the IDS).

Desrosiers (Nature Medicine. March, 2004; 10 (3): 221-223) review the current state of the HIV vaccine art and provides several explanations for the lack of development of an HIV vaccine. These include the ineffectiveness of the natural immune response to infection, the lack of an animal model, the inability to protect related primates from similar viruses, the lack of

protection against heterologous viral infection and the resistance of HIV to neutralization in a phase 3 vaccine trial. Desrosiers state that it is currently unknown what kind of an immune response would be effective against infection, how to elicit neutralizing antibodies against the virus or how to overcome obstacles due to HIV sequence variability.

The level of skill of one in the art

While it is within the skill of one in the art to make monoclonal antibodies 6E10 and 5B3 and elicit an immune response with them, it is beyond the skill of one in the art to make the instant Mabs 13H8, 6D8 and 5B6 due to the lack of public availability of the hybridomas used to produce these antibodies (discussed above). It is also beyond the skill of on in the art to identify an antibody or an epitope-binding fragment thereof, required by claims 19 and 26, which shares the characteristics of the specific antibodies 6E10, 13H8 and 6D8 because the "characteristics" intended are not clearly defined. Finally, it is beyond one skilled in the art to use the instant antibodies claimed in a pharmaceutical composition to induce a therapeutic or prophylactic immune response because there is no disclosure provided for how one would overcome the immune inefficiencies in the prior art of a candidate vaccine, discussed by Berman et al., or current obstacles in the HIV vaccine art, discussed by Desrosiers.

The level of predictability in the art

The assertion of therapeutic and prophylactic requirements, set forth in the instant method claim 23, necessarily requires evidence to support applicant's assertion. Since the art does not disclose any ameliorative or preventive HIV agents, the skilled artisan would not

predict, in the absence of proof to the contrary, that the monoclonal antibodies instantly claimed are efficacious as an HIV vaccine.

The amount of direction provided by the inventor

There is insufficient guidance provided which describe the "characteristics" of the instant monoclonal antibodies or what effect these antibodies would have on a host *in vivo*. Claim 23 requires a therapeutically acceptable dose of one of the instant monoclonal antibodies claimed. The only reference to administration of the antibodies is on page 38, lines 26-36. A therapeutically acceptable amount is defined as an amount that restores T cell counts. However, there is no teaching provided for what amounts are intended to be administered, how much would be sufficient to restore T cell counts or whether the restoration of T cells would be therapeutically effective for an infected patient or prophylactic to a patient at risk of infection, which are required by the claim. There is insufficient guidance to provide the skilled artisan with sufficient guidance to practice the nature of the invention.

The existence of working examples

There are no working examples demonstrating the administration of the instant antibodies. There is also no data provided that would indicate any therapeutic or preventative properties of the monoclonal antibodies in an HIV-infected patient.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught

one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). There is not seen in the disclosure, sufficient evidence to support the instant claims of prevention or treatment of HIV with the instant antibodies. There are also no working examples or data in the art that would provide a nexus between the effectiveness of the instant composition and method claimed and an HIV vaccine. For these reasons, it is determined that the instant claims would require an undue quantity of experimentation of one skilled in the art to make and use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19 and 26 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Berman et al. (Journal of Virology. 1989; 63 (8): 3489-3498, provided in the IDS).

Claims 19 and 26 require a monoclonal antibody that has characteristics of antibody 6E10, 13H8 or 6D8. The instant antibodies inhibit the interaction between gp120 and CD4, see page 5, lines 36-37 of the instant disclosure, and neutralize viruses *in vitro*, see Table 4 for example.

The antibodies in the sera of Berman et al. clearly anticipate these characteristics, see Table 1 and Figure 6 on page 3495. Therefore, the antibodies of Berman et al. clearly anticipate antibodies possessing the characteristics of the antibodies instantly claimed.

Claims 19 and 26 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Lasky et al. (Cell. 1987; 50: 975-985, provided in the IDS).

Claims 19 and 26 require a monoclonal antibody that has characteristics of antibody 6E10, 13H8 or 6D8. The instant antibodies block the binding of gp120 and CD4, see page 5, lines 36-37 of the instant disclosure.

Lasky et al. teach monoclonal antibodies, 5C2E5 and 7F11, that block the interaction between gp120 and the CD4 receptor, see "Isolation of gp120..." and Figure 4 on page 977. Since the antibodies of Lasky et al. clearly anticipate a characteristic shared by the instant antibodies claimed, the antibodies of Lasky et al. clearly anticipate claims 19 and 26.

Claims 19 and 26 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Matsushita et al. (Journal of Virology. 1988; 62 (6): 2107-2114).

The disclosure indicates that the instant Mabs are specific for the region of HIV gp120 that contains an internal clip site, which is approximately amino acids 285-286 of a mature gp120 and 315-316 of an HIV-IIIB comprising the N-terminal signal sequence, see page 5, lines 27-34 and page 10, lines 16-36. These antibodies block the binding of gp120 and CD4, see page 5, lines 36-37.

Matsushita et al. clearly anticipate antibodies that bind to the amino acids 315-316, disclosed, see Figure 6 on page 2112 for example. It is noted that the teachings of Matsushita et al. is admitted prior art on page 62, lines 1-3 of the instant disclosure.

Claims 19 and 26 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Javaherian et al. (PNAS. 1989; 86: 6768-6772, provided in the IDS).

Javaherian et al. teach a major neutralizing epitope spanning the clip site instantly disclosed. The reference also teaches Mabs that specifically bind to this site and inhibit fusion between CD4 and gp160, see the entire reference and especially the paragraph bridging pages 6770-6771.

Claims 19-22 and 26-28 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dowbenko et al. (Journal of Virology. 1988; 62 (12): 4703-4711).

The claims are drawn to Mab 6D8 bound to a marker and/or a toxin and in a pharmaceutical carrier. The claims also require a cell culture or hybridoma comprising an antibody that has the characteristics of 6D8.

Dowbenko et al. clearly anticipate monoclonal antibodies to gp120 and instant Mab 6D8 instantly claimed, see the entire reference and Table 1 on page 4705 for example. The Mabs of Dowbenko et al. are labeled, are in a pharmaceutically acceptable vehicle and are bound to a toxin (periodate-oxidized glycerol-coated control pore glass), see columns 1 and 2 on page 4704. Dowbenko et al. clearly anticipate a hybridoma that yields Mab 6D8, see the first paragraph on page 4704.

Claims 19-21 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Remington et al. (US 4,361,647).

Claims 19 and 26 require a monoclonal antibody that has characteristics of antibody 6E10, 13H8 or 6D8. Claim 20 states that antibody 5B6 is bound to a detectable marker and claim 21 states that antibody 5B6 is in a pharmaceutically acceptable carrier.

Remington et al. anticipate a monoclonal antibody 5B6, see column 10, lines 46-50. Since the characteristics intended in claim 19 are indeterminable, the monoclonal antibody of Remington appears to possess the characteristics required by the claim. A sample from the hybridoma producing 5B6 of Remington et al. is injected into mice, see column 9, lines 21-35, and labeled, see column 9, lines 55-61.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dowbenko et al. *supra*.

The claim is drawn to a specific hybridoma with an ATCC accession number to produce Mab 6D8. Although Dowbenko et al. do not teach the specific accession number for the hybridoma, the reference clearly teaches a hybridoma that is equivalent to the instant one asserted to be deposited since the 6D8 monoclonal antibody of Dowbenko et al. and the 6D8 monoclonal antibody instantly claimed are indistinguishable.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Remington et al. as applied to claims 19-21 and 26 above, and further in view of Reading et al. (US 4,474,893).

The claim states that the antibody is conjugated to a toxin.

See the teachings of Remington et al. above. The reference does not teach conjugating the Mab to a toxin.

However, Reading et al. teach conjugating Mabs with a toxin for specific delivery and minimize the interaction with other cells, see column 2, lines 45-63.

One of ordinary skill in the art at the time the invention was made would have been motivated to conjugate the 5B6 Mab of Remington et al. with the toxin of Reading et al. to reduce nonspecific interaction of the Mab with cells upon administration. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for conjugating 5B6 Mab with the toxin of Reading et al. because both Remington et al. and Reading et al. induce immune responses with Mabs from hybridomas, see the previous citations of Remington et al. and column 4, line 51 to column 6, line 20 and column 7, lines 26-29 of Reading et al. for example.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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